

REMARKS

Reconsideration of this application is respectfully requested in view of the foregoing amendments and the following remarks.

Sequence Listing:

The Examiner requests that if the sequence listing of record filed on November 26, 2004 is not the correct sequence listing, then Applicants should submit another sequence disclosure. As the specification was amended in response to the last Office Action, Applicants necessarily amended the sequence listing to conform to the amended specification. Submitted concurrently with this amendment is an electronic text file of the SEQUENCE LISTING for the above-identified application submitted under 37 C.F.R. § 1.821(e) and a Statement to Support Filing and Submission. Applicants respectfully request that the electronic copy of the sequence listing be entered into the application. The electronic file contains no new matter (37 C.F.R. § 1.821 (g)). Support for the electronic sequence listing is found in the application as filed and in the sequence listing of record filed on November 26, 2004.

Applicants do not believe a paper copy is required at this time. If the Examiner further requires a paper copy, please inform the undersigned.

Amendments to the Claims

Claims 6-8, 11, 13-14, and 24-26 are pending. This response amends claims 7, 11, 25, and 26, cancels claim 8, and adds new claims 29-30. All of the claims, including the amendments, are shown in the previous section. Applicants submit that the amendments do not introduce new matter. Specifically, claims 7, 11, 25, and 26 are amended to reflect elected subject matter. New claim 29 depends from claim 6 and identifies one means for improving functionality as a means for enhancing thermostability. This claim is supported by, for example, page 3, lines 23-24; page 8, line 9; page 14, line 12; pages 16-18, Table 2; and pages 20-21, Table 5 of Appendix A, submitted June 22, 2006. New claim 30 depends from claim 26, and describes further cellobiohydrolase mutations. This claim is supported by claim :

Response to Examiner's Arguments

Response to Objection of June 22, 2006 Amendment under 35 U.S.C. § 132 (a)

The Examiner objects to the amended specification and asserts that the amendment introduces new matter. The Examiner requests that Applicants point out specifically where the added material is supported by the priority documents or the original specification.

On page 2 of Appendix B (submitted on June 22, 2006), the first sentence of the last paragraph, Applicants refer to SEQ ID NO: 5 as representing CBH 1 protein from *Trichoderma reesei*. The incorporation of the SEQ ID NO into this paragraph is supported by the specification as originally filed. Specifically, Figure 1 displays the coding sequence of the *cbh I* gene. This same sequence is represented by SEQ ID NO: 4 in the sequence listing. Translation of SEQ ID NO: 4 generates SEQ ID NO: 5 of the sequence listing. Thus, reference to SEQ ID NO: 5 in the specification merely aids in the understanding of the disclosure and is not new matter.

On page 4 of Appendix B, lines 7-8 of the fourth full paragraph, Applicants refer to three CBH-1 variants and their respective SEQ ID NOs: 6, 7, and 8. The incorporation of these SEQ ID NOs into this paragraph is supported by the specification as originally filed. Specifically, these variants have the same sequence as SEQ ID NO: 5 except that each has an Asn to Ala amino acid substitution at the 45th, 270th, and 384th residues respectively. Example 4 describes the production of the single site substituted mutants in the *cbh I* coding sequence represented by SEQ ID NO: 4 (See the originally filed specification at, for example, pages 11-13). The molecular weights of the CBH 1 single site mutant proteins are shown in Table 1 and demonstrate that the substitution from Asn to Ala reduces molecular weight relative to the wild type proteins (See originally filed specification at page 13). The SEQ ID NOs are also supported by the nucleic acid sequences shown in Table 4 where the Asn to Ala mutations are shown in the mutagenic sense strand (See originally filed specification at page 18). Upon translation, each polypeptide sequence shows the critical amino acid residue of the CBH-1 protein that was substituted. Thus, reference to SEQ ID NOs: 6, 7, and 8 in the specification aids the reader's understanding of the disclosure and is not new matter.

On page 5 of Appendix B, the description of Figure 4 is amended to change the SEQ ID NOs and to incorporate the sequences from the Figure. The nucleic acid sequence now represented by SEQ ID NO: 1 is shown in Figure 4. Similarly, the amino acid sequence now represented by SEQ ID NO: 2 is the translation of SEQ ID NO: 1 and also shown in Figure 4.

Thus, reference to SEQ ID NOs: 1 and 2 in the specification and Replacement Figure 4 is not new matter.

On page 6 of Appendix B, lines 5 and 7 have been amended to properly include SEQ ID NOs 9 and 97. Inclusion of SEQ ID NOs does not add new matter as the sequences were disclosed in the specification as filed.

Response to Rejection of Claim 6 under 35 U.S.C. 4 112, First Paragraph

The Examiner rejects claim 6 under 35 U.S.C. § 112, First Paragraph, as not described in the specification in such a way that enables one skilled in the art to make or use the invention. Specifically, the Examiner asserts that the "any mutation [of the cellobiohydrolase] that will improve any functionality" is overly broad and the claim should be limited to embodiments taught in the specification. Applicants respectfully disagree.

When determining whether a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue", the following factors can be considered: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In *re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). These factors are taken into consideration in the arguments below.

The phrase "improved functionality" is characterized as an improvement in the function of a variant cellulase enzyme relative to the native cellulase enzyme produced by *Trichoderma reesei* (page 3, lines 12-15). One of skill in the art would know and have access to assays in which the activity of enzymes in various conditions would be compared.

Throughout the specification Applicants point out aspects of improved functionality including improved thermal stability (page 3, lines 23-24; page 8, line 9; page 14, line 12; pages 16-18, Table 2; and pages 20-21, Table 5 of Appendix A, submitted June 22, 2006), improved protein stability (page 15, line 3 of Appendix A), decreased peptide strain (page 15, line 4 and page 18, Table 3 of Appendix A), improved helix propensity (page 15, lines 5-6 of Appendix A), decreased degrees of rotational freedom (page 15, lines 25-27 of Appendix A), decreased product inhibition (page 4, lines 27-28 and pages 18-19, Table 3b of Appendix A), and decreased glycosylation (page 8, line 8; page 13, line 1; and page 20, Table 4 of Appendix A). These

improvements are not overly broad but are directed to functions relevant to the cellobiohydrolase 1 gene.

Examples 1-6 demonstrate how improved variants were obtained and sequences provided indicate exemplary mutations made to achieve improved functionality. Therefore, claim 6 is enabled according to the Wands factors described above as Applicants have provided more than sufficient direction in the specification and provided multiple examples describing the improved variants, because the quantity of experimentation needed to make or use the improved variants is limited based on the Applicants' disclosure, and because the level of one of ordinary skill in the art is such that assays for determining enzymatic activity are well known.

Response to Rejection of Claims 7-8, 11, and 26 under 35 U.S.C. § 112, Second Paragraph

The Examiner rejects claims 7-8, 11, and 26 under 35 U.S.C. § 112, second paragraph for containing embodiments not elected for prosecution. Applicants have amended these claims to reflect the previous election of Group 1, and respectfully request withdrawal of this rejection.

Response to Objection of Claims 13-14 and 24-25 as Dependent upon Rejected Claims

The Examiner objects to claims 13-14 and 24-25 as being dependent upon rejected base claims. Applicants believe that the amendments to the base claims overcome the 35 U.S.C. § 112, second paragraph rejection, thus mooting the objection to claims 13-14 and 24-25. As such, Applicants respectfully request withdrawal of this rejection.

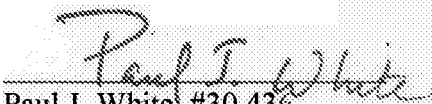
Summary

For the reasons set forth above, Applicants respectfully submit the claims are allowable and reconsideration and issuance of a notice of allowance are respectfully requested. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 14-0460 if not otherwise specifically requested. The undersigned hereby authorizes the charge of any required fees not included or any deficiency of fees submitted herewith to be charged to deposit account No. 14-0460.

Respectfully submitted,

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